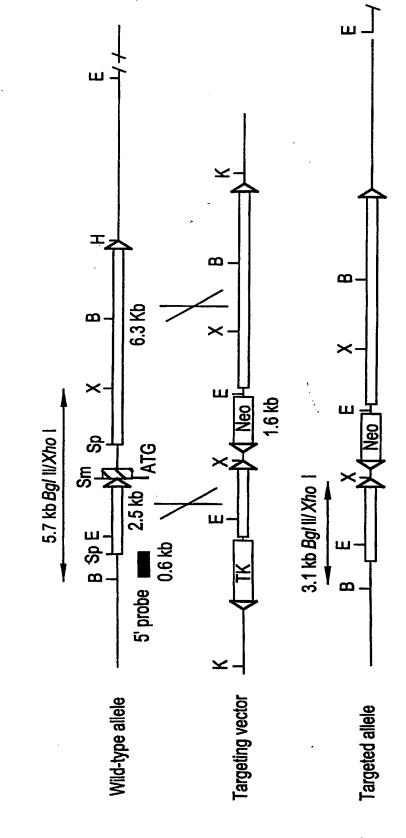
FIG. 1A



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FIG. 1B

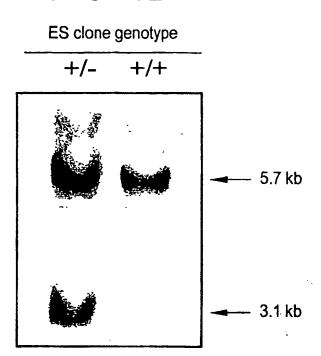


FIG. 1C

М

+/+ -/-- Wt allele - Targeted allele

FIG. 1D

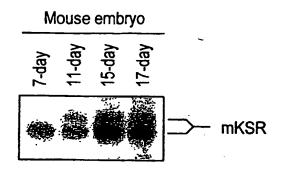


FIG. 1E

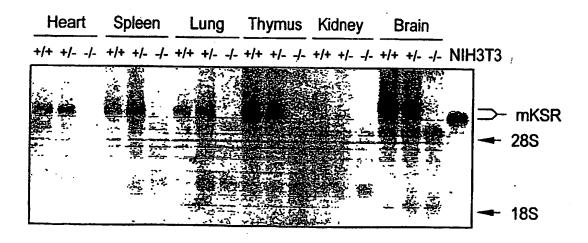
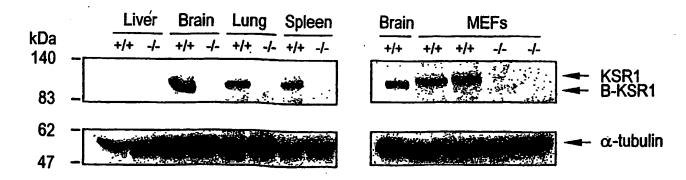
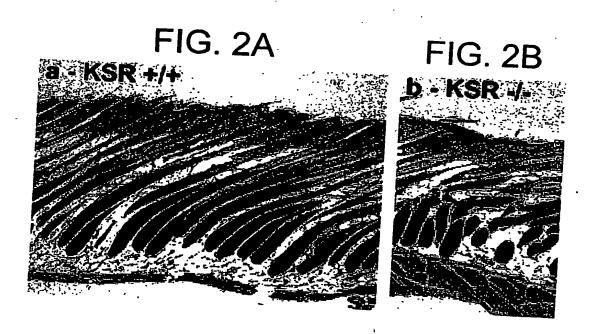
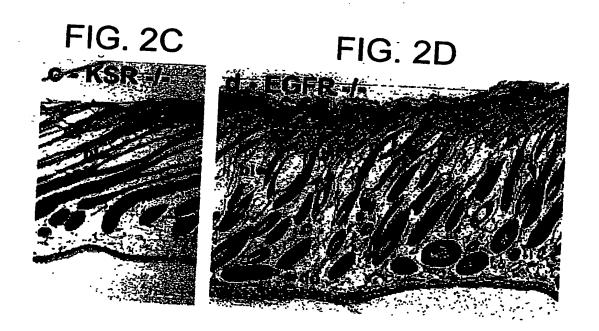


FIG. 1F







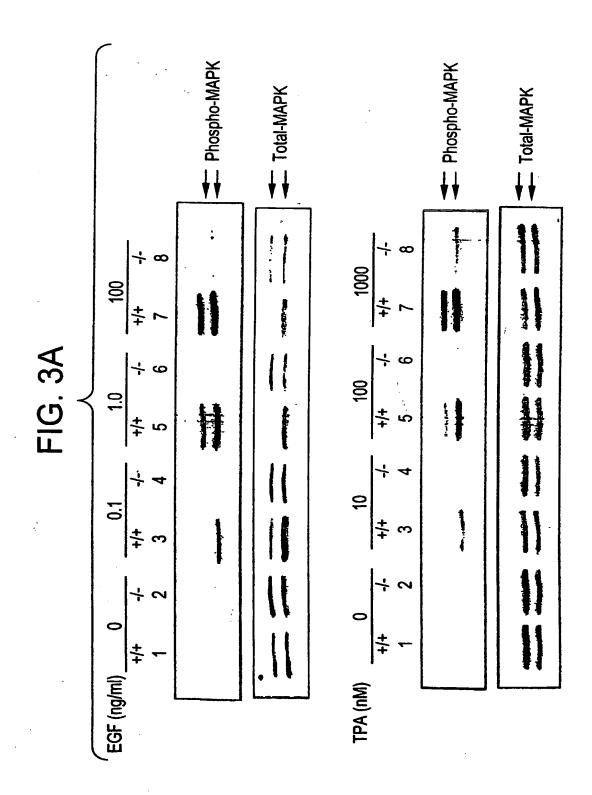


FIG. 3B

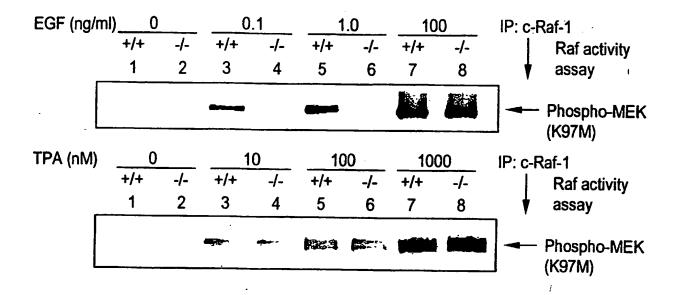


FIG. 3C

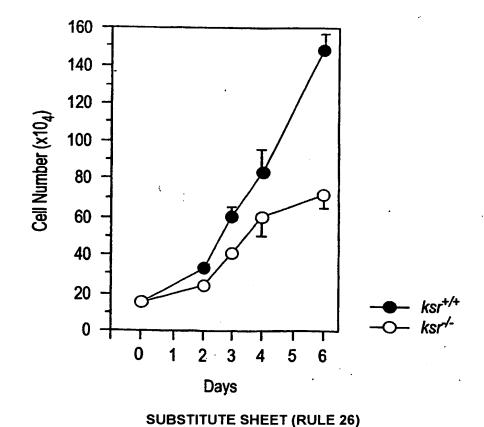
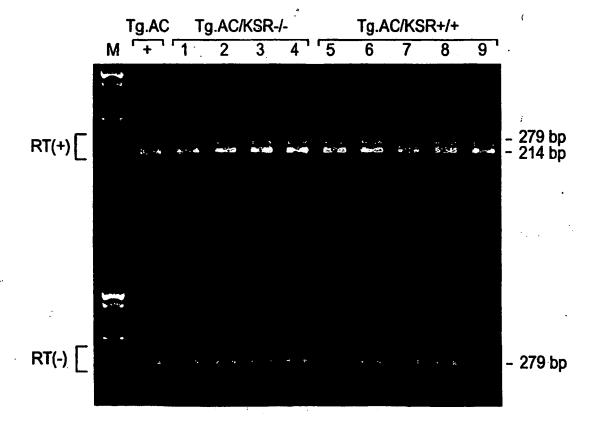


FIG. 4A



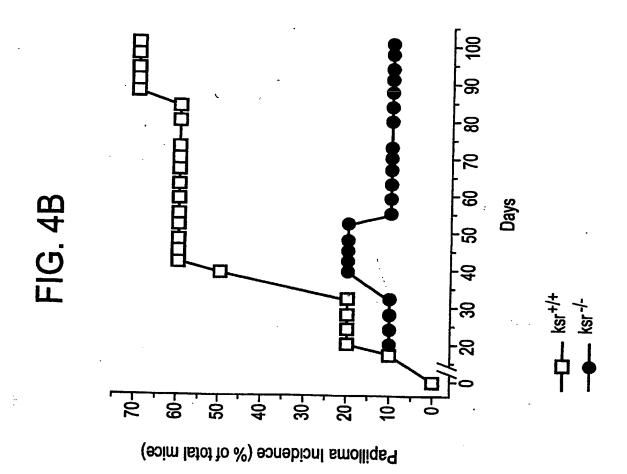


FIG. 5A

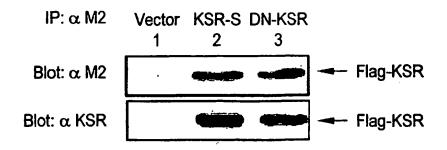


FIG. 5B

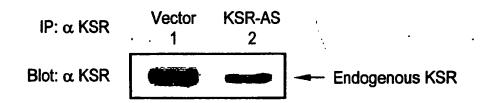
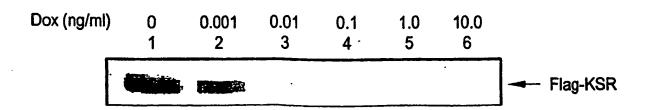
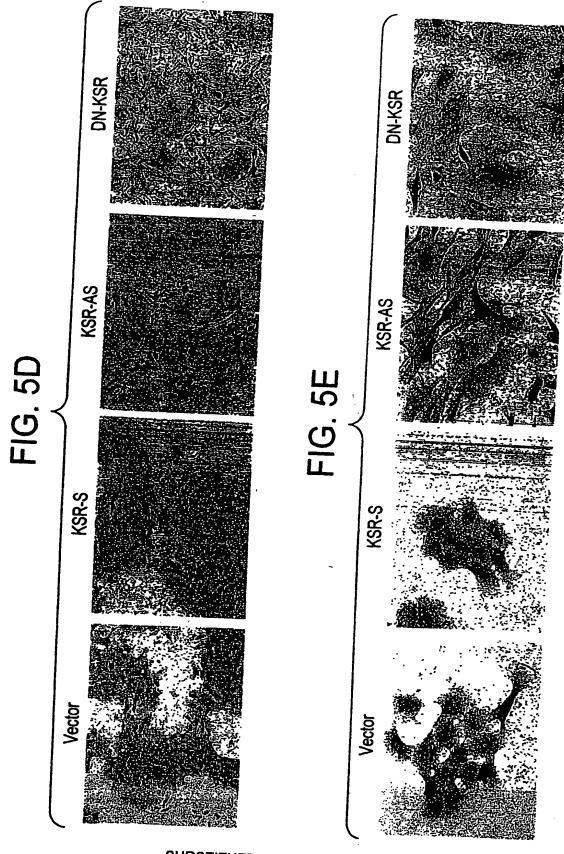


FIG. 5C



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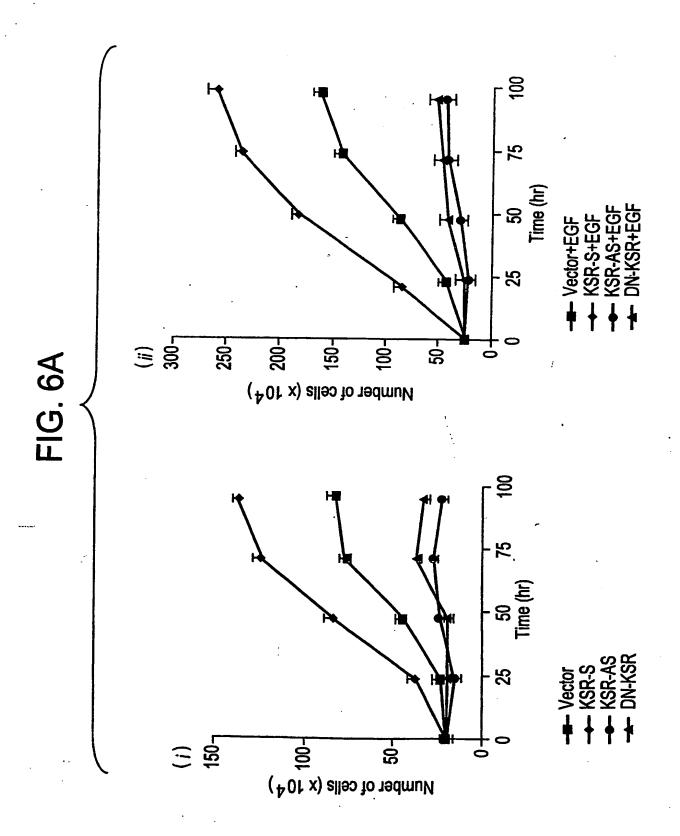
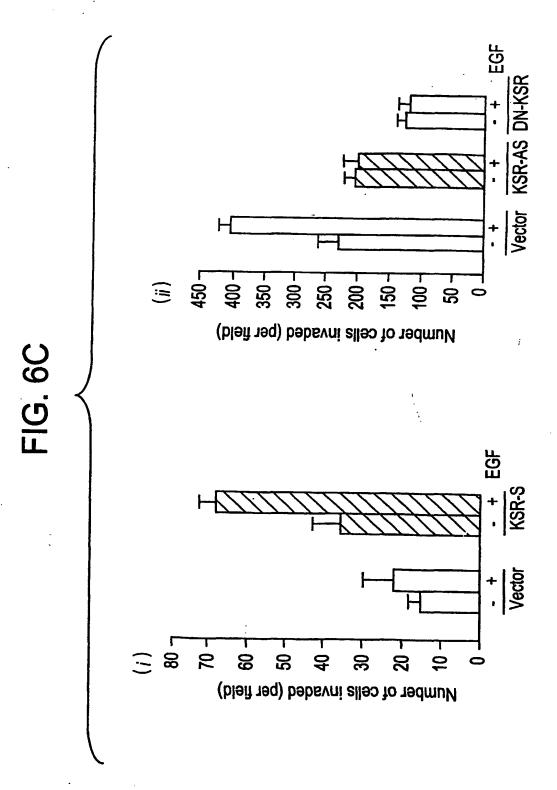
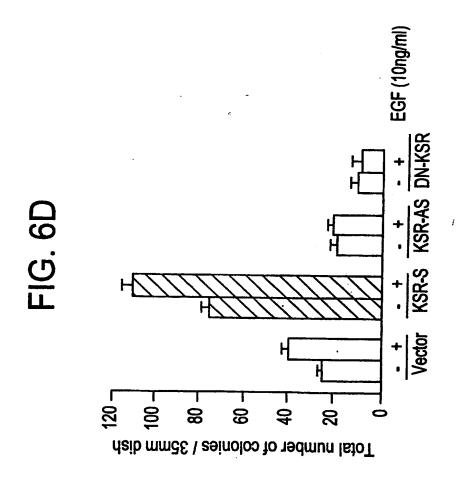


FIG. 6B

•	% G1	8%	% G2
Vector	40.1	45.1	14.8
KSR-S	25.2	8.09	14.0
KSR-AS	16.4	23.2	60.4
DN-KSR	24.2	24.8	51.0







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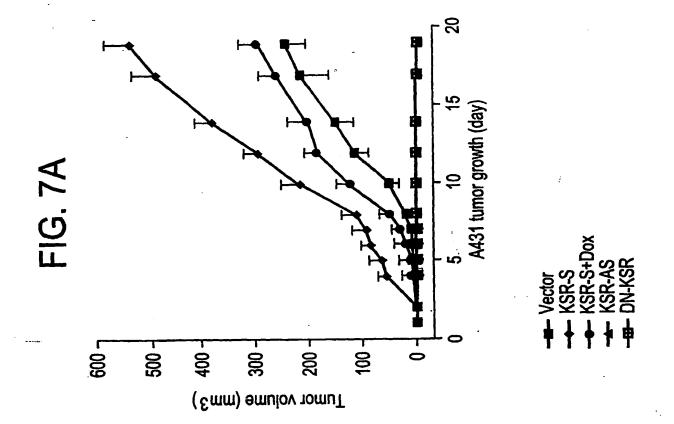
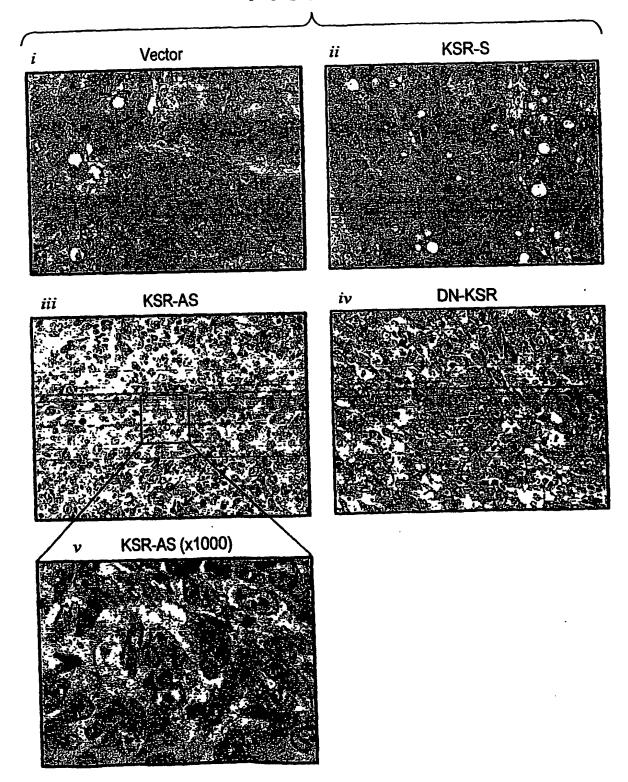
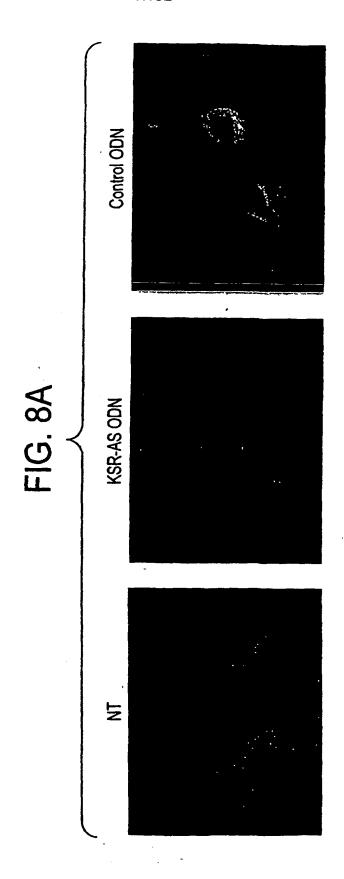
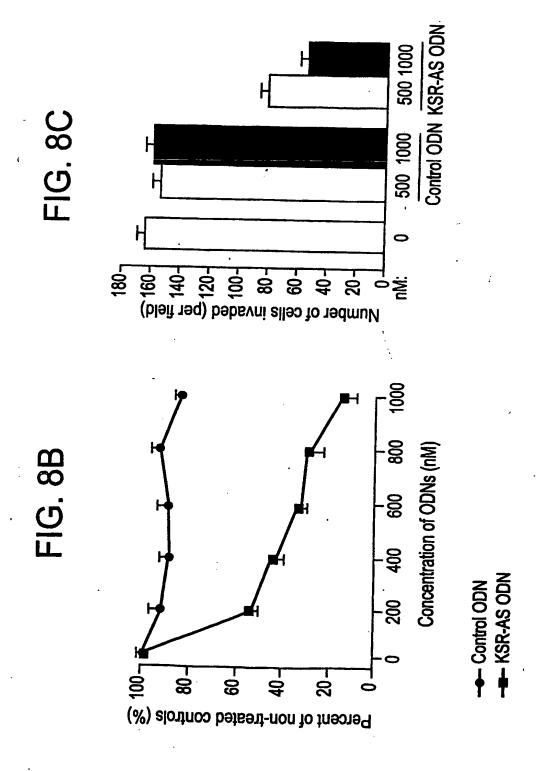


FIG. 7B



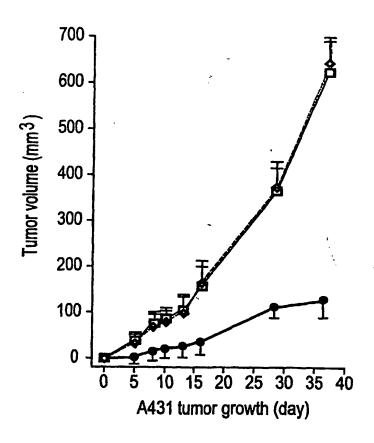


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FIG. 8D



- -□- Saline
- Control ODN KSR-AS ODN

Fig. 9A

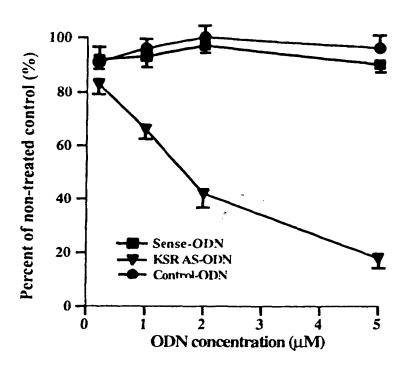
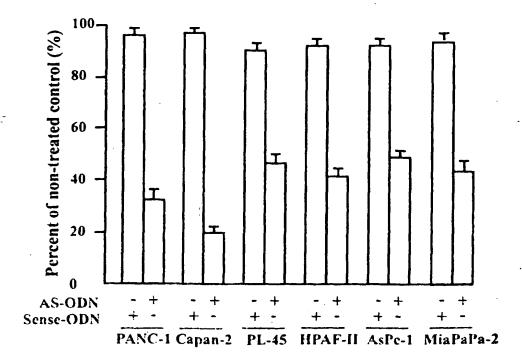
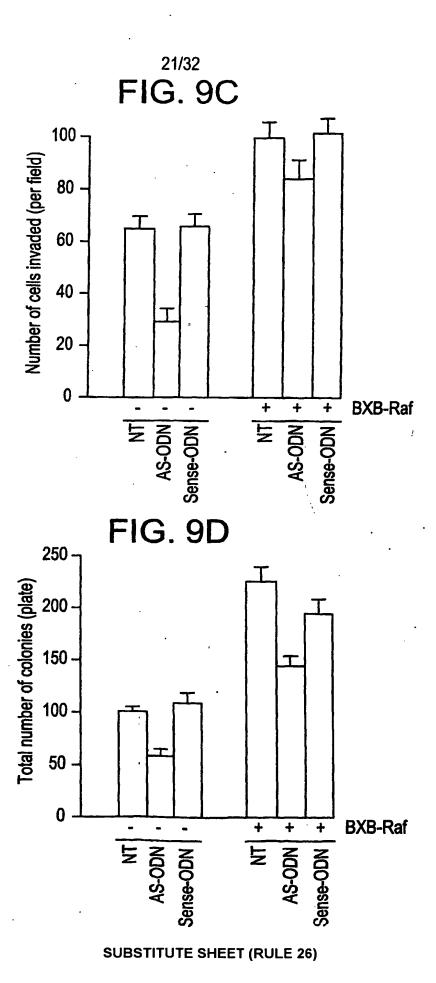


Fig. 9B





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FIG. 9E

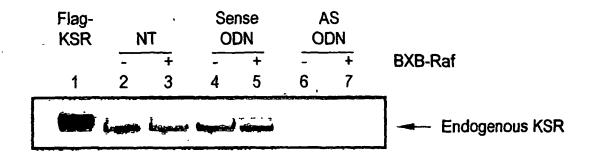
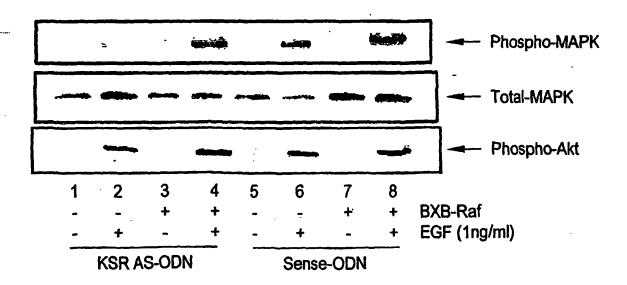
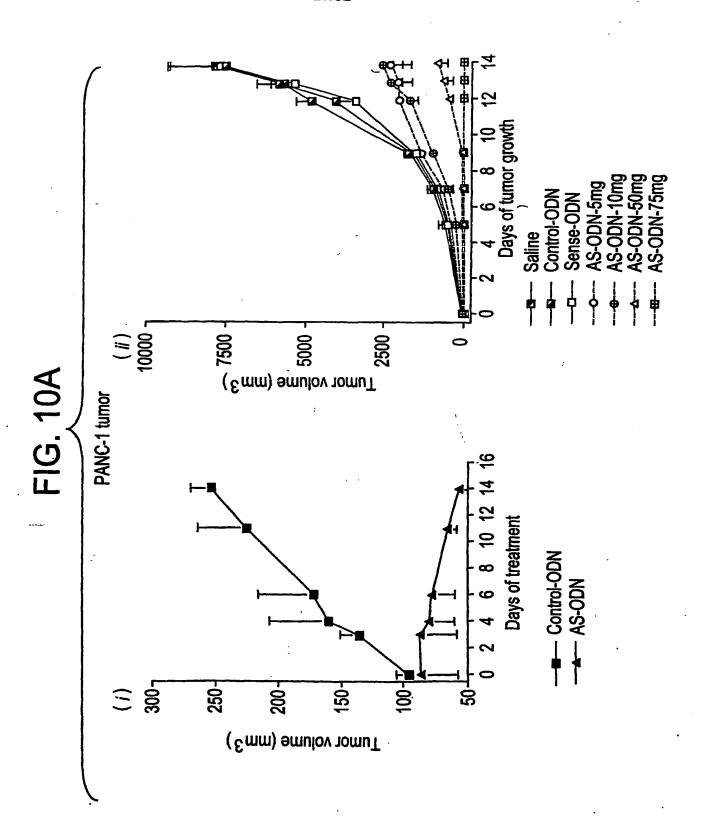


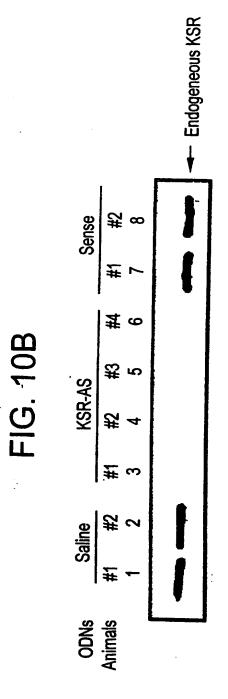
FIG. 9F

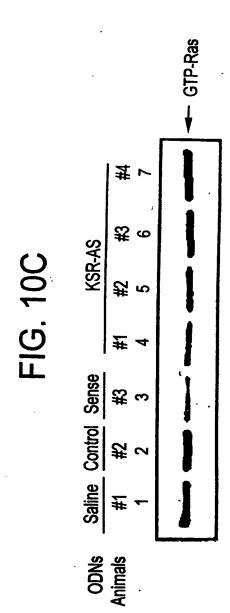


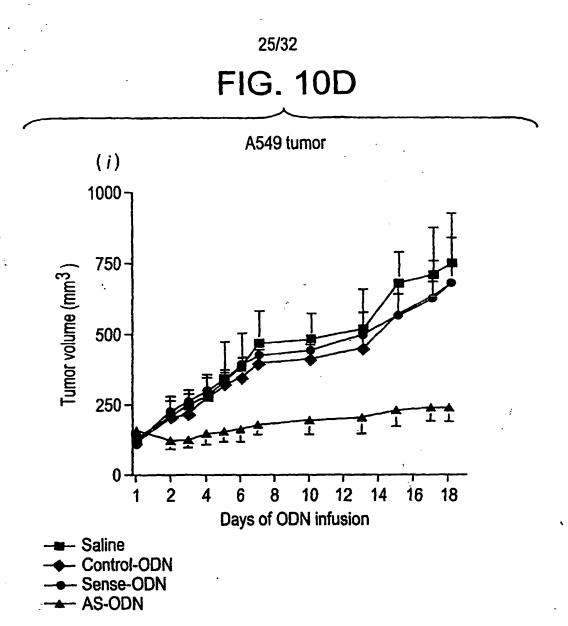




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(ii) Number of lung metastases foci (whole lung surface)

Dose of infusion (mg/ kg /Day)	Sense-ODNs	AS-ODN	% inhibition	
10	7.4 ± 1.4	2.5 ± 0.6	65	
25	10.2 ± 1.8	1.4 ± 0.5	86	

Human Mouse	MGEK-EGGGGDAAAAEGGAGAAASRALQQCGQ <u>LQ</u> MDRAALRAAA K V	34
Human Mouse	CA1 KLIDISTGSLRGLRTKCAVSNDLTOOEIRTLEAKLVRYICKQRQC K Q S	79
Human Mouse	KLSVAPGERTPELNSYPRFSDWLYTFNVRPEVVQEIPRDLTLDAL I SD A I QE	124
Human Mouse	LEMNEAKVKETLRRCGASGDECGRLQYALTCLRKVTGLGGEHKED D A M W TE S Q M	169
Human Mouse	SSWSSLDARRESGSGPSTDTLSAASLPWPPGSSQLGRAGNSAQGP G I DS -L PM M S A T	214
Human Mouse	RSISVSALPASDSPTPSFSECLSDTCIPLHASGRLTPRALHSFIT V GL S I	259
Human Mouse	CA2 PPTTPQLRRHTKLKPPR <u>TPPPPSRKVFOLL</u> PSFPTLTRRKSHESQ A	i 304
Human Mouse	LGNRIDDVSSMRFDLSHGSPQMVRRDIGL <u>SVTHRFSTKSWLSOVC</u> TP K E P L	349
Human Mouse	CA3 HVCOKSMIFGVKCKHCRLKCHNKCTKEAPACRISFLPLTRLRRTE N I A	394
Human Mouse	SVPSDINNPVDRAAEPHFGTLPKALTKKEHPPAMNHLDSSSNPSS -	439 ⁻
Human Mouse	CA4 TTSSTPSSPAPFPTSSNPSSATTPPNPSPGORDSRFNFPAAYFIH L S	484
Human Mouse	HROOFIFPDISAFAHAAPLPEAADGTRLDDQPKADVLEAHEAEAE CSC SST S I GV	529
Human Mouse	EPEAGKSEAEDDED-EVDDLPSSRRPWRGPISRKASQTSVYLQEW ED	573

Fig. 11-1

FIG. 11-2

	I	
Human Mouse	DDIPFEQVELGEPIGQGRWGRVHRGRWHGEVAIRLLEMDGHNQDH	618
Human Mouse	III IV V LKLFKKEVMNYRQTRHENVVLFMGACMNPPHLAIITSFCKGRTLH	663
Human Mouse	VIa VIb SFVRDPKTSLDINKTRQIAQEIIKGMGYLHAKGIVHKDLKSKNVF	708
Human Mouse	VII VIII YDNGKVVITDFGLFGISGVVREERRENQLKLSHDWLCYLAPEIVR	753
	IX	
Human Mouse	EMTPGKDEDQLPFSKAADVYAFGTVWYELQARDWPLKNQAAEASI I R F H P L X XI	798
Human Mouse	WQIGSGEGMKRVLTSVSLGKEVSEILSACWAFDLQERPSFSLLMD VR A G	843
Human Mouse	MLEKLPKLNRRLSHPGHFWKSAEL R DINSSKVMPRFERFGLGTLESGN	867
Mouse	PKM	

FIG. 12A-1

1	GAATTCCCTC	GGGGCTTTCC	TGCCGAGGCG	CCCGTGTCCC	CGGGCTCCTC	GCCTCGGCCC
61	CCAGCGGCCC	CGATGCCGAG	GCATGGATAG	AGCGGCGTTG	CGCGCGGCAG	CGATGGGCGA
121	GAAAAAGGAG	GGCGGCGGCG	GGGCGCCGC	GGCGGACGGG	GGCGCAGGGG	CCGCCGTCAG
181	CCGGGCGCTG	CAGCAGTGCG	GCCAGCTGCA	GAAGCTCATC	GATATCTCCA	TCGGCAGTCT
241	GCGCGGGCTG	CGCACCAAGT	GCTCAGTGTC	TAACGACCTC	ACACAGCAGG	AGATCCGGAC
301	CCTAGAGGCA	AAGCTGGTGA	AATACATTTG	CAAGCAGCAG	CAGAGCAAGC	TTAGTGTGAC
3.61	CCCAAGCGAC	AGGACCGCCG	AGCTCAACAG	CTACCCACGC	TTCAGTGACT	GGCTGTACAT
421	CTTCAACGTG	AGGCCTGAGG	TGGTGCAGGA	GATCCCCCAA	GAGCTCACAC	TGGATGCTCT
481	GCTGGAGATG	GACGAGGCCA	AAGCCAAGGA	GATGCTGCGG	CGCTGGGGGG	CCAGCACGGA
541	GGAGTGCAGC	CGCCTACAGC	AAGCCCTTAC	CTGCCTTCGG	AAGGTGACTG	GCCTGGGAGG
601	GGAGCACAAA	ATGGACTCAG	GTTGGAGTTC	AACAGATGCT	CGAGACAGTA	GCTTGGGGCC
661	1				AGCACTCAGG	
721					CCCGGCCTCA	· · · ·
781	CTCGGACTCC	TGTATCCCCT	TGCACACCAG	CGGCCGGCTG	ACCCCCGGG	CCCTGCACAG
841					GCCAAGCTGA	
901					CCCAGCTTCC	
961					GACGACGTCA	
1021					GATATCGGGC	
					AACGTGTGCC	
					CATAACAAGT	
					CTTCGGAGGA	
					CCCCATTTTG	
					CTGGACTCCA	
				,	TTCCTGACCT	·
		-	-		CGGGACAGCA	
					AGCACAGCCG	
					GAAGCAGAGG	
					GAGGTGGACG	
					AGCCAGACCA	
					GAGCCCATTG	
				•	GCCATTCGGC	
1861	GGACGGCCAC	AATCAGGACC	ACCTGAAGCT	GTTCAAGAAA	GAGGTGATGA	ACTACCGGCA
1921	GACGCGGCAT	GAGAACGTGG	TGCTCTTCAT	GGGGGCCTGC	ATGAACCCAC	CTCACCTGGC
					TTCGTGAGGG	
		· · · · · · · · · · · · · · · · · · ·			ATCATCAAGG	
					AAGAATGTCT	
					TCGGGTGTGG	
					TGCTACCTGG	
					CCCTTCTCCA	
					AGAGACTGGC	
					GAAGGAGTAC	
					TCTGCCTGCT	
					CTGGAGAGGC	
					GCTGACATTA	
					GAGTCCGGTA	

FIG. 12A-2

2701	GTAGCCAGCC	CTGCACGTTC	ATGCAGAGAG	TGTCTTCCTT	TCGAAAACAT	GATCACGAAA
2761	CATGCAGACC	ACCACCTCAA	GGAATCAGAA	GCATTGCATC	CCAAGCTGCG	GACTGGGAGC
2821	GTGTCTCCTC	CCTAAAGGAC	GTGCGTGCGT	GCGTGCGTGC	GTGCGTGCGT	GCGTGCGTCA
2881	CCAAGGTGTG	TGGAGCTCAG	GATCGCAGCC	ATACACGCAA	CTCCAGATGA	TACCACTACC
2941	GCCAGTGTTT	ACACAGAGGT	TTCTGCCTGG	CAAGCTTGGT	ATTTTACAGT	AGGTGAAGAT
3001	CATTCTGCAG	AAGGGTGCTG	GCACAGTGGA	GCAGCACGGA	TGTCCCCAGC	CCCCGTTCTG
3061	GAAGACCCTA	CAGCTGTGAG	AGGCCCAGGG	TTGAGCCAGA	TGAAAGAAAA	GCTGCGTGGG
3121	TGTGGGCTGT	ACCCGGAAAA	GGGCAGGTGG	CAGGAGGTTT	GCCTTGGCCT	GTGCTTGGGC
3181	ÇGAGAACCAC	ACTAAGGAGC	AGCAGCCTGA	GTTAGGAATC	TATCTGGATT	ACGGGGATCA
3241	GAGTTCCTGG	AGAGTGGACT	CAGTTTCTGC	TCTGATCCAG	GCCTGTTGTG	CTTTTTTTTT
3301	TTCCCCCTTA	AAAAAAAAA	AGTACAGACA	GAATCTCAGC	GGCTTCTAGA	CTGATCTGAT
3361	GGATCTTAGC	CCGGCTTCTA	CTGCGGGGGG	GAGGGGGGA	GGGATAGCCA	CATATCTGTG
3421	GAGACACCCA	CTTCTTTATC	TGAGGCCTCC	AGGTAGGCAC	AAAGGCTGTG	GAACTCAGCC
3481	TCTATCATCA	GACACCCCCC	CCCAATGCCT	CATTGACCCC	CTTCCCCCAG	AGCCAAGGGC
3541	TAGCCCATCG	GGTGTGTGTA	CAGTAAGTTC	TTGGTGAAGG	AGAACAGGGA	CGTTGGCAGA
3601	AGCAGTTTGC	AGTGGCCCTA	GCATCTTAAA	ACCCATTGTC	TGTCACACCA	GAAGGTTCTA
3661	GACCTACCAC	CACTTCCCTT	CCCCATCTCA	TGGAAACCTT	TTAGCCCATT	CTGACCCCTG
3721	TGTGTGCTCT	GAGCTCAGAT	CGGGTTATGA	GACCGCCCAG	GCACATCAGT	CAGGGAGGCT
3781	CTGATGTGAG	CCGCAGACCT	CTGTGTTCAT	TCCTATGAGC	TGGAGGGGCT	GGACTGGGTG
3841	GGGTCAGATG	TGCTTGGCAG	GAACTGTCAG	CTGCTGAGCA	GGGTGGTCCC	TGAGCGGAGG
3901	ATAAGCAGCA	TCAGACTCCA	CAACCAGAGG	AAGAAAGAAA	TGGGGATGGA	GCGGAGACCC
3961	ACGGGCTGAG	TCCCGCTGTG	GAGTGGCCTT	GCAGCTCCCT	CTCAGTTAAA	ACTCCCAGTA
4021	AAGCCACAGT	TCTCCGAGCA	CCCAAGTCTG	CTCCAGCCGT	CTCTTAAAAC	AGGCCACTCT
4081	CTGAGAAGGA	ATTC		•		

FIG. 12B-1

1	GCGAAGCTGG	TCCGTTACAT	TTGTAAGCAG	AGGCAGTGCA	AGCTGAGCGT	GGCTCCCGGT
61	GAGAGGACCC	CAGAGCTCAA	CAGCTACCCC	CGCTTCAGCG	ACTGGCTGTA	CACTTTCAAC
121	GTGAGGCCGG	AGGTGGTGCA	GGAGATCCCC	CGAGACCTCA	CGCTGGATGC	CCTGCTGGAG
181	ATGAATGAGG	CCAAGGTGAA	GGAGACGCTG	CGGCGCTGTG	GGGCCAGCGG	GGATGAGTGT
241	GGCCGTCTGC	AGTATGCCCT	CACCTGCCTG	CGGAAGGTGA	CAGGCCTGGC	TTCATCACCC
301	CGCCCACCAC	ACCCCAGCTG	CGACGGCACA	CCAAGCTGAA	GCCACCACGG	ACGCCCCCC
361	CACCCAGCCG	CAAGGTCTTC	CAGCTGCTGC	CCAGCTTCCC	CACACTCACC	CGGAGCAAGT
421	CCCATGAGTC	TCAGCTGGGG	AACCGCATTG	ATGACGTCTC	CTCGATGAGG	TGAGTTGGGA
481	GCACGTTCCT	GCACGTGGCT	ATGCTGTGGG	GCCTCTCTCA	TGAGTCAGAG	CGGAGGGAGA
541	CAGCTGTGCC	TCTGGAGTCT	GCTTTTAATT	GTCTGGAAAT	GCAGAGATGT	CTGGTTTTTG
601	CCTGAGCAAA	ATAGGAGTTT	ATTTTTGTAC	TATCCCGAGC	TGGCTAAGGA	GAGTCACGTA
661	GCTGTGGGCG	GGGTCTTGGG	GATGAGGAGG	GGTACAGCAG	GCAGGGACTA	TGCTGAAGTG
721	GAGCTGGCTG	TAGGAACCCC	AGGGAGGCAC	AGGGGGAGCA	TGAAGAGGAG	CTACACTTCC
781	CTCCCTTAGT	GCCCGGGCAG	AAACTCCCAG	GGCCCTTCAC	AGAACCTTGG	AGGAACATTC
841	AACACCCCCA	TCTCTAGGAC	AGCCCCAGCC	TTGTCATCCT	CCAATTGCTG	TGGTAACACG
901	GGGACTGGAG	CAGTGAGATT	ATTAGGCCTT	CAGGGCCAGT	GTCTCCATGC	AGATCAGATG
961	GAGGCGGTGC	TTGGCACATA	CACCACCTCA	CTGCCCATGC	CCCCAGAAGT	TGGTGCAGAT
1021	CATAAGGTGG	CTTTTGGGGC	TAATTGATTG	AAGTTCCAAC	ATAGTCTGTT	TCTCCTAGGC
1081	TGGTAGCTGG	CACCTTTGGC	CCCATGTGTT	TTTTAATTAT	TTTTTCTTTT	GAGACGAAAT
1141	CTCGCTCTAT	CACCCAGGCT	GAAGTGCAGT	AGTGCAATCT	CAGCTCACTG	CAGCCTCTGC
1201	CTCCCGGGTT	CAAGCAATTC	TCCTGCCTCA	GCCTCCCGAG	TAGCCAGGAT	TAAAGGTGCC
1261	TGCCACCACA	CATGGCTAAT	TTTTGTATTT	TTAATAGAGA	CGGGGTTTCA	CCATGTTAGC
1321	CAGGCTGGTC	TCAAACTCCT	GACCTCAGGT	GATCTTCCTG	CCTCAGCCTC	CCAAAGTGCT
1381	GGGATTACAG				GTGTTTTGGT	GGTCTTGGCT
1441	GCTGATGGGT	GGGGTGAGCC	CCAGGAGGAA	GTTGGGACAA	GTCAACCTCA	TGGCAGATGT
1501	GCCAGGGAGA	GCTGCGGGTG	AGATAGATTG	TTCCTATCCC	CCTCTCCTTG	ATGTGGGAGG
1561	ACTCAGTACC		CCTTCTCATG			TGGCCTCAAG
1621			CCAGCTTTGT			TGAGGGGGGC
1681	AGTGGCCACC	CTCGGGGGAC	CTTCTGACTC	AGAGGACATG		
1741			GTCACAGGTC		TTGGATGAAA	GTCTTAGATC
1801	<u>.</u> .		ACAACATTCT		TCCAGAGGGT	TCCCGGACCC
	CCGAAGCCCA				CTGAGTATGG	GGGCATCTCT
1921	CGCATGGATC				GTCGGTGACG	CACAGGTTCT
1981			CAGGTCTGCC			
2041			TTGAAGTGTC			GCCCCTGCCT
2101	GTAGAATATC		•			CCCTCGGACA
2161			GCAGCCGAAC			AAAGCACTGA
2221	CAAAGAAGGA	GCACCCTCCG	GCCATGAATC	ACCTGGACTC	CAGCAGCAAC	CCTTCCTCCA
2281	CCACCTCCTC	CACACCCTCC	TCACCGGCGC	CCTTCCCGAC	ATCATCCAAC	CCATCCAGCG

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FIG. 12B-2

2341	CCACCACGCC	CCCCAACCCC	TCACCTGGCC	AGCGGGACAG	CAGGTTCAAC	TTCCCAGCTG
2401	CCTACTTCAT	TCATCATAGA	CAGCAGTTTA	TCTTTCCAGA	CATTTCAGCC	TTTGCACACG
2461	CAGCCCCGCT	CCCTGAAGCT	GCCGACGGTA	CCCGGCTCGA	TGACCAGCCG	AAAGCAGATG
2521	TGTTGGAAGC	TCACGAAGCG	GAGGCTGAGG	AGCCAGAGGC	TGGCAAGTCA	GAGGCAGAAG
2581	ACGATGAGGA	CGAGGTGGAC	GACTTGCCGA	GCTCTCGCCG	GCCCTGGCGG	GGCCCCATCT
			AGCGTGTACC			
2701	TAGAGCTGGG	CGAGCCCATC	GGGCAGGGCC	GCTGGGGCCG	GGTGCACCGC	GGCCGCTGGC
2761	ATGGCGAGGT	GGCCATTCGC	CTGCTGGAGA	TGGACGGCCA	CAACCAGGAC	CACCTGAAGC
			AACTACCGGC			
			CCCCACCTGG			
			GACCCCAAGA			
			GGCATGGGAT			
			TTCTATGACA			
			GTCCGAGAGG			
			GCCCCTGAGA			
			AAAGCTGCTG			
			CCCTTGAAGA			
			AAGCGTGTCC			
			TGGGCTTTCG			
			CTTCCCAAGC			
			TAGGCCTGGC			
			CGTGACTTCT			
			GCTGCTCCAG	- ·		
3721	TGTTTTAAAA	ACTGGCCCTC	TGCCCTCTCC	ACGTGGCCTG	CATATGCCCA	AG

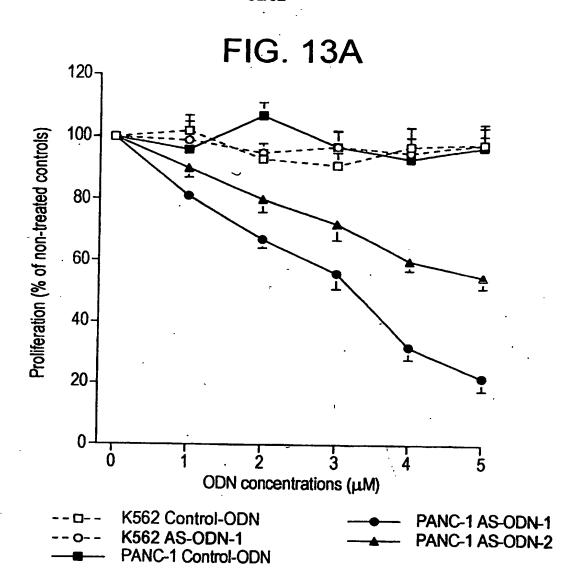


FIG. 13B

